

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year)

05 July 2001 (05.07.01)

International application No.

PCT/JP00/06226

Applicant's or agent's file reference

FP-PC-0018

International filing date (day/month/year)

12 September 2000 (12.09.00)

Priority date (day/month/year)

13 September 1999 (13.09.99)

Applicant

TAKAI, Yoshihiro et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

11 April 2001 (11.04.01)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
 34, chemin des Colombettes
 1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

H. Zhou

Telephone No.: (41-22) 338.83.38



INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference FP-PC-0018	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/ JP 00/ 06226	International filing date (day/month/year) 12/09/2000	(Earliest) Priority Date (day/month/year) 13/09/1999
Applicant POLA CHEMICAL INDUSTRIES, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D233/91 A61K49/00 A61K51/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	WADA, HIROAKI ET AL: "Synthesis of 1-'2-'18F!fluoro-1-(hydroxymethyl)-ethoxy! methyl-2- nitroimidazole ('18F!FENI), a potential agent for imaging hypoxic tissues by PET" J. LABELLED COMPD. RADIOPHARM. (2000), 43(8), 785-793 , July 2000 (2000-07), XP002167863 abstract; figure 1; examples 2,18F2 --- -/--	1-11

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *8* document member of the same patent family

Date of the actual completion of the international search

18 May 2001

Date of mailing of the international search report

07/06/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Seitner, I

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>ALAUDDIN M M ET AL: "Evaluation of 9-⁹-(3-F-fluoro-1-hydroxy-2-propoxy)methyl guanine (⁹F!-FHPG) in vitro and in vivo as a probe for PET imaging of gene incorporation and expression in tumors - Initial evaluation with PET with the radiolabeled glucose analogue 2-(F-18)fluoro-2-deoxy-d-glucose" NUCLEAR MEDICINE AND BIOLOGY,US,ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY, vol. 26, no. 4, May 1999 (1999-05), pages 371-376, XP004167069 ISSN: 0969-8051 page 372, paragraphs 1,2 abstract tables 1,2</p>	1-11
Y	<p>US 5 728 843 A (CHERIF ABDALLAH ET AL) 17 March 1998 (1998-03-17) abstract; examples 1A,1B figures 1,2</p>	1-11
A	<p>J E BISKUPIK ET AL: "Synthesis of an (iodovinyl)misonidazole Derivative for hypoxia imaging" JOURNAL OF MEDICINAL CHEMISTRY,US,AMERICAN CHEMICAL SOCIETY. WASHINGTON, vol. 34, 1991, pages 2165-2168, XP002091797 ISSN: 0022-2623 abstract; table 1</p>	1-11
A	<p>TEWSON T J: "Synthesis of ⁹F!Fluoroetanidazole: A Potential New Tracer for Imaging Hypoxia" NUCLEAR MEDICINE AND BIOLOGY,US,ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY, vol. 24, no. 8, 1 November 1997 (1997-11-01), pages 755-760, XP004097016 ISSN: 0969-8051 abstract; figures 1,5-8</p>	1-11
A	<p>US 5 843 404 A (KOCH CAMERON J ET AL) 1 December 1998 (1998-12-01) examples 1,6</p>	1-11

-/--

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>ALAUDDIN M M ET AL: "Synthesis and Preliminary Evaluation of 9-(4-¹⁸F-Fluoro-3-Hydroxy methylbutyl)Guanine (¹⁸F!FHBG): A New Potential Imaging Agent for Viral Infection and Gene Therapy Using PET - Synthesis of 9-¹⁸-(1-F-fluoro-3-hydroxy-2-propoxy)-methyl !guanine"</p> <p>NUCLEAR MEDICINE AND BIOLOGY,US,ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY, vol. 25, no. 3, 1 April 1998 (1998-04-01), pages 175-180, XP004113272 ISSN: 0969-8051 page 177, column 2 abstract</p> <p>---</p>	1-11
A	<p>EP 0 312 858 A (POLA CHEM IND INC) 26 April 1989 (1989-04-26) example 3</p> <p>-----</p>	1-9

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 8 and 9 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No

Information on patent family members

T/JP 00/06226

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5728843	A	17-03-1998	US 5886190 A	23-03-1999
			AU 8074294 A	01-05-1995
			WO 9509844 A	13-04-1995
<hr/>				
US 5843404	A	01-12-1998	US 5540908 A	30-07-1996
			CA 2149770 A	26-05-1994
			EP 0669913 A	06-09-1995
			JP 8503469 T	16-04-1996
			WO 9411348 A	26-05-1994
<hr/>				
EP 0312858	A	26-04-1989	JP 1110675 A	27-04-1989
			JP 2115626 C	06-12-1996
			JP 8019111 B	28-02-1996
			CA 1329392 A	10-05-1994
			DE 3868308 A	19-03-1992
			ES 2032514 T	16-02-1993
			KR 9611379 B	22-08-1996
			US 4945102 A	31-07-1990
			US 5064849 A	12-11-1991
<hr/>				

PATENT COOPERATION TREATY

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

From the INTERNATIONAL BUREAU

To:

ARUGA, Mitsuyuki
Kyodo Building
3-6, Nihonbashiningyocho 1-chome
Chuo-ku
Tokyo 103-0013
JAPON



Date of mailing (day/month/year) 06 November 2000 (06.11.00)	
Applicant's or agent's file reference FP-PC-0018	IMPORTANT NOTIFICATION
International application No. PCT/JP00/06226	International filing date (day/month/year) 12 September 2000 (12.09.00)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 13 September 1999 (13.09.99)
Applicant POLA CHEMICAL INDUSTRIES, INC. et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
3. An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
4. The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
13 Sept 1999 (13.09.99)	11/259057	JP	27 Octo 2000 (27.10.00)
14 Sept 1999 (14.09.99)	11/260315	JP	27 Octo 2000 (27.10.00)

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. (41-22) 740.14.35</p>	<p>Authorized officer</p> <p>Magda BOUACHA</p> <p>Telephone No. (41-22) 338.83.38</p>
---	---

PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTICE INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

ARUGA, Mitsuyuki
Kyodo Building
3-6, Nihonbashiningyocho 1-chome
Chuo-ku
Tokyo 103-0013
JAPON



Date of mailing (day/month/year) 22 March 2001 (22.03.01)		
Applicant's or agent's file reference FP-PC-0018		IMPORTANT NOTICE
International application No. PCT/JP00/06226	International filing date (day/month/year) 12 September 2000 (12.09.00)	Priority date (day/month/year) 13 September 1999 (13.09.99)
Applicant POLA CHEMICAL INDUSTRIES, INC. et al		

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:

AU, KP, KR, US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE, AG, AL, AM, AP, AT, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EA, EE, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OA, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 22 March 2001 (22.03.01) under No. WO 01/19799

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a **demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.


For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer J. Zahra Telephone No. (41-22) 338.83.38
--	---

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference FP-PC-0018		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/JP00/06226	International filing date (day/month/year) 12/09/2000	Priority date (day/month/year) 13/09/1999	
International Patent Classification (IPC) or national classification and IPC C07D233/00			
Applicant POLA CHEMICAL INDUSTRIES, INC. et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application 			
Date of submission of the demand 11/04/2001		Date of completion of this report 26.11.2001	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Stix-Malaun, E Telephone No. +49 89 2399 8057	



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP00/06226

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):
Description, pages:

1-18 as originally filed

Claims, No.:

1-11 as originally filed

Drawings, sheets:

1/1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/JP00/06226

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 6-9.

because:

☒ the said international application, or the said claims Nos. 6-9(Industrial Applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims 1-11

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP00/06226

	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-11
Industrial applicability (IA)	Yes:	Claims	1-5,10,11
	No:	Claims	

2. Citations and explanations
see separate sheet

III NON-ESTABLISHMENT

Claims 6-9 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

V REASONED STATEMENT

1. PRIOR ART

The documents cited in the International Search Report

D1: ALAUDDIN M M ET AL: 'Evaluation of 9-[(3-F-fluoro-1-hydroxy-2-propoxy)methyl] guanine ([F]-FHPG) in vitro and in vivo as a probe for PET imaging of gene incorporation and expression in tumors - Initial evaluation with PET with the radiolabeled glucose analogue 2-(F-18)fluoro-2-deoxy-d-glucose' NUCLEAR MEDICINE AND BIOLOGY,US,ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY, vol. 26, no. 4, May 1999 (1999-05), pages 371-376, XP004167069 ISSN: 0969-8051

D2: US-A-5 728 843 (CHERIF ABDALLAH ET AL) 17 March 1998 (1998-03-17)

have been considered for the examination procedure.

2. NOVELTY

The claimed subject-matter is considered to be novel:

The essential structural difference between the claimed compounds and those of D1 or D2 resides in the presence of the 2-nitro-1-propoxymethyl - substituted imidazole unit. D1 lacks the isolated imidazole unit which is substituted by nitro in position 2, D2 lacks the (sulfonyl)propoxymethyl substituent in position 1.

Therefore the compounds of claim 1, their use and preparation and the

intermediates of claim 10 are rendered novel (Article 33(2) PCT).

3. INVENTIVE STEP

The subject-matter of the present application does not fulfil the requirements of Article 33(3) PCT for the following reasons:

The technical problem may be seen in the provision of novel imidazole derivatives which are useful for imaging cancer cells or ischemic sites of circulatory organs (see description p. 3).

The closest prior art is represented by D2.

D2 discloses compounds which are also useful for imaging tumor cells (see abstract).

As already stated above present compounds differ from those of D2 merely due to the substituent in position 1 of the imidazole unit which is 3-fluor-1-hydroxy-2-propoxymethyl instead of 3-fluor 2-hydroxy-propyl (see fig. 1, compound 1A).

D1 (see abstract, tables 1,2) discloses guanine derivatives of the same use. Position 9 of the guanine unit which corresponds to position 1 in the isolated imidazole unit is substituted also by the 3-fluor-1-hydroxy-2-propoxymethyl moiety.

Facing the problem discussed above and taking into consideration the teachings of D1 and D2 a skilled person would expect that compounds which represent a combination of the two structural features (isolated 2-nitro-imidazole moiety of D2 and 3-fluor-1-hydroxy-2-propoxymethyl substituent of D1) which are well known in the field of tumor diagnosis exhibit the alleged quality.

Therefore the presently claimed solution seems to be obvious in view of the cited prior art.

With respect to the remaining independent claims no inventive contribution over the prior art can be detected.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/JP00/06226

Therefore an inventive step cannot be acknowledged.

4. INDUSTRIAL APPLICABILITY

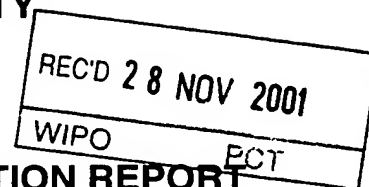
For the assessment of the present Claims 6-9 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference FP-PC-0018		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) FOR FURTHER ACTION	
International application No. PCT/JP00/06226	International filing date (day/month/year) 12/09/2000	Priority date (day/month/year) 13/09/1999	
International Patent Classification (IPC) or national classification and IPC C07D233/00			
Applicant POLA CHEMICAL INDUSTRIES, INC. et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 11/04/2001	Date of completion of this report 26.11.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Stix-Malaun, E Telephone No. +49 89 2399 8057 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP00/06226

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-18 as originally filed

Claims, No.:

1-11 as originally filed

Drawings, sheets:

1/1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/JP00/06226

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 6-9.

because:

☒ the said international application, or the said claims Nos. 6-9(Industrial Applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims 1-11

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/JP00/06226

	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-11
Industrial applicability (IA)	Yes:	Claims	1-5,10,11
	No:	Claims	

2. Citations and explanations
see separate sheet

III NON-ESTABLISHMENT

Claims 6-9 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

V REASONED STATEMENT

1. PRIOR ART

The documents cited in the International Search Report

D1: ALAUDDIN M M ET AL: 'Evaluation of 9-[(3-F-fluoro-1-hydroxy-2-propoxy)methyl] guanine ([F]-FHPG) in vitro and in vivo as a probe for PET imaging of gene incorporation and expression in tumors - Initial evaluation with PET with the radiolabeled glucose analogue 2-(F-18)fluoro-2-deoxy-d-glucose' NUCLEAR MEDICINE AND BIOLOGY,US,ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY, vol. 26, no. 4, May 1999 (1999-05), pages 371-376, XP004167069 ISSN: 0969-8051

D2: US-A-5 728 843 (CHERIF ABDALLAH ET AL) 17 March 1998 (1998-03-17)

have been considered for the examination procedure.

2. NOVELTY

The claimed subject-matter is considered to be novel:

The essential structural difference between the claimed compounds and those of D1 or D2 resides in the presence of the 2-nitro-1-propoxymethyl - substituted imidazole unit. D1 lacks the isolated imidazole unit which is substituted by nitro in position 2, D2 lacks the (sulfonyl)propoxymethyl substituent in position 1.

Therefore the compounds of claim 1, their use and preparation and the

intermediates of claim 10 are rendered novel (Article 33(2) PCT).

3. INVENTIVE STEP

The subject-matter of the present application does not fulfil the requirements of Article 33(3) PCT for the following reasons:

The technical problem may be seen in the provision of novel imidazole derivatives which are useful for imaging cancer cells or ischemic sites of circulatory organs (see description p. 3).

The closest prior art is represented by D2.

D2 discloses compounds which are also useful for imaging tumor cells (see abstract).

As already stated above present compounds differ from those of D2 merely due to the substituent in position 1 of the imidazole unit which is 3-fluor-1-hydroxy-2-propoxymethyl instead of 3-fluor 2-hydroxy-propyl (see fig. 1, compound 1A).

D1 (see abstract, tables 1,2) discloses guanine derivatives of the same use. Position 9 of the guanine unit which corresponds to position 1 in the isolated imidazole unit is substituted also by the 3-fluor-1-hydroxy-2-propoxymethyl moiety.

Facing the problem discussed above and taking into consideration the teachings of D1 and D2 a skilled person would expect that compounds which represent a combination of the two structural features (isolated 2-nitro-imidazole moiety of D2 and 3-fluor-1-hydroxy-2-propoxymethyl substituent of D1) which are well known in the field of tumor diagnosis exhibit the alleged quality.

Therefore the presently claimed solution seems to be obvious in view of the cited prior art.

With respect to the remaining independent claims no inventive contribution over the prior art can be detected.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

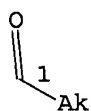
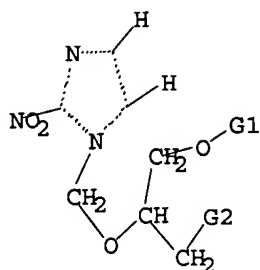
International application No. PCT/JP00/06226

Therefore an inventive step cannot be acknowledged.

4. INDUSTRIAL APPLICABILITY

For the assessment of the present Claims 6-9 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

=> d l1
 L1 HAS NO ANSWERS
 L1 STR



G1 H, [01]

G2 F, SO2

Structure attributes must be viewed using STN Express query preparation.

=> d his

(FILE 'HOME' ENTERED AT 09:22:57 ON 11 JUN 2003)

FILE 'REGISTRY' ENTERED AT 09:23:05 ON 11 JUN 2003

L1 STRUCTURE UPLOADED
 L2 0 S L1
 L3 4 S L1 FULL
 L4 4 S L3 AND CAPLUS/LC
 L5 0 S L3 AND CAOLD/LC

FILE 'CAPLUS' ENTERED AT 09:24:16 ON 11 JUN 2003

L6 3 S L3